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(71) Applicant: **Cabrera Garrido, Juan**
Calle Porton de Tejeiro, 2
E-18005 Granada (ES)
Applicant: **Cabrera Garcia-Olmedo, Juan**
Calle Porton de Tejeiro, 2
E-18005 Granada (ES)

(72) Inventor: **Cabrera Garrido, Juan**
Calle Porton de Tejeiro, 2
E-18005 Granada (ES)
Inventor: **Cabrera Garcia-Olmedo, Juan**
Calle Porton de Tejeiro, 2
E-18005 Granada (ES)

(74) Representative: **Herrmann-Trentepohl, Werner, Dipl.-Ing.**
Patentanwälte Herrmann-Trentepohl, Kirschner, Grosse, Bockhorni & Partner
Forstenrieder Allee 59
D-81476 München (DE)

(54) INJECTABLE MICROFOAM CONTAINING A SCLEROSING AGENT.

(57) Injectable microfoam for sclerotherapy. The sclerotherapy of varices is based on the injection of liquid substances capable of suppressing them. The present invention relates to the preparation of sclerosing substances in the form of a microfoam. The microfoam is prepared with sclerosing agents, and is then injected in the vein to be treated, so that the microfoam displaces the blood contained in the vein and provides for the contact of the sclerosing agent with the vascular endothelium, with a predetermined known concentration and during a controllable time.

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State of the art

Sclerosis of varicose veins is based on the injection into the veins of liquid substances which, by causing a localized inflammatory reaction, favours the elimination of these abnormal veins.

When a sclerosing liquid is injected, it is mixed with the blood contained in the vein and is diluted in an unkonwn proportion. The results are uncertain (owing to over- or under-dosage) and are limited to short varicose segments.

As the size of the varicose veins to be injected decreases, this dilution is less and the results obtained are more predictable. Nowadays, sclerosis is a technique selected in cases of small and medium varicose veins, those with diameters equal to or greater than 7 mm being treated by surgery.

At present, sclerosis and surgery complement one another but sclerosis treatment continues not to be applicable to large varicose veins.

In these large varicose veins, if a sclerosing substance is injected, its concentration in the vein, its homogeneous distribution in the blood, and the time for which it is in contact with the internal walls of the vessel treated are not known.

In 1946, Orbach injected a few cubic centimetres of air into small varicose eins and confirmed a displacement of the blood inside the vessel which was occupied by the injected air. The sclerosing solution introduced immediately afterwards was more effective than if it had been injected into the blood.

In thick varicose veins, when air is injected the phenomenon described of the displacement of the blood by the injected air does not occur but the air forms a bubble inside the vein which makes the method ineffective in these vessels.

The same author had the idea, a few years later, of injecting foam obtained by agitation of a container containing sodium tetradecyl sulphate, which is an anionic sclerosing detergent with a good foaming capability.

The method was of little use owing to the large size of the bubbles formed and was dangerous owing to the side effects of atmospheric nitrogen which is only slightly soluble in blood.

Both methods had limited practical repercussion being used only in small varicose veins.

Description of the invention

This invention relates to the preparation of a sclerosing micro-foam.

According to the present invention, it has been discovered that if a micro-foam of a pharmacologically inert, sterile, physiological serum is injected in a horizontal position, the micro-foam causes displacement of the blood contained in the vessel, including the most expanded varicose veins, on account of the low pressure of the blood contained therein in the horizontal.

The elevation of the member injected reduces the venous pressure even more facilitating the filling of the vein exclusively with micro-foam, which remains in the vessel as long as the patient does not get up from the operating table.

If the micro-foam produced with the physiological serum is replaced by micro-foam produced with a sclerosing substance and injected into the vein, it displaces the blood contained in the vein and ensures that the sclerosing agent contacts the endothelium of the vessel in a known concentration and for a controllable time, achieving sclerosis of the entire segment occupied.

The advantages of this method allow:

1. the concentration of the sclerosing agent in the vessel to be known, since the micro-foam displaces the blood and is not diluted therein like a liquid;
2. homogeneous distribution of the sclerosis product therein to be insured,
3. the time for which it is kept in contact with the internal walls of the vein to be controlled;

none of wich factors is known precisely or is controllable with the use of liquid sclerosing agents.

The present invention can be implemented by the preparation of a micro-foam with any sclerosing substance such as: polydocanol, sodium tetradecyl sulphate, hypertonic glucose or gluco-saline solutions, chromic glycerol, ethanolamine oleate, sodium morrhuato, or iodic solutions.

Once the sclerosing micro-foam has been produced by any of the existing methods, of which two are descried below, it is introduced into any sterile container which can serve for subsequent injection into the veins to be treated and which permits stability of the foam in a form which can be extracted by means of a syringe or any other instrument which facilitates its injection into the vessels to be treated.

Example 1:

The sclerosing micro-foam was produced by mixing in a sterile, hermetic container connected, if desired, to a pressure bottle of oxygen, or a mixture of oxygen and carbon dioxide or other physiological gases; mechanical heating was carried out by means of a micro-motor which rotated a brush immersed in the sclerosing solution to be foamed.

The micro-foam was produced by heating at between 8,000 and 15,000 rpm for a period of between 60 and 120 seconds.

It was introduced into any container which could later serve for its storage and its subsequent injection into the vessels to be sclerosed.

If the sclerosing substance does not have a foaming capability, polysorbate 20, polysorbate 80, polygelina or any other substance with a foaming capability accepted as inert for intravenous use is added.

Example 2:

The sclerosing substance was introduced into a hermetic, pressurized and sterile container and the micro-foam was produced by stirring the solution with discharge from the container for subsequent use.

Claims

1. An injectable micro-foam for therapeutic uses, prepared or for preparation as required, **characterized in that** the micro-foam is produced with any sclerosing substance.

2. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the sclerosing substance is polycadonol.

3. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the sclerosing substance is sodium tetradecyl sulphate.

4. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the sclerosing substance is a hypertonic glucose or gluco-saline solution.

5. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the substance used is chromic glycerol.

6. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the substance used is ethanolamine oleate.

7. An injectable micro-foam for therapeutic uses according to claim 1, **characterized in that** the substance used is sodium morrhuate.

8. An injectable micro-foam for therapeutic uses 1, **characterized in that** the sustance used is any iodic suolution.

9. An injectable micro-foam for therapeutic uses according to the preceding claims, **characterized by** its use in phlebology.

10. An injectable micro-foam for therapeutic uses according to claims 1 to 8, **characterized by** its use in the treatement of oesophageal varices.

11. An injectable micro-foam for therapeutic uses according to claims 1 to 8, **characterized by** its use in proctology.

12. An injectable micro-foam for therapeutic uses according to claims 1 to 8, **characterized by** its use in angiology.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/ES 94/00064

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61K9/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO,A,92 05806 (SINTETICA S.A.) 16 April 1992 see claim 1	1-12
A	EP,A,0 077 752 (SCHERING AKTIENGESELLSCHAFT) 27 April 1983 see claim 1	1-12

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Ventura Amat, A

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INTERNATIONAL SEARCH REPORT

information on patent family members

Int onal Application No
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